US-PAT-NO: 6429017

DOCUMENT-IDENTIFIER: US 6429017 B1

TITLE: Method for predicting the presence of haemostatic dysfunction in a patient sample

DATE-ISSUED: August 6, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Toh; Cheng Hock	Liverpool	N/A	N/A	GB
Downey; Colin	Liverpool	N/A	N/A	GB
Fischer; Timothy J.	Raleigh	NC	N/A	N/A

APPL-NO: 09/ 372954

DATE FILED: August 12, 1999

PARENT-CASE:

This application is a continuation-in-part of U.S. patent application Ser. No. 09/244,340, filed Feb. 4, 1999, the subject matter of which is incorporated herein by reference. This application also relates to U.S. Pat. No. 5,646,046 to Fischer et al., the subject matter of which is incorporated herein by reference.

US-CL-CURRENT: 436/69, 422/73 , 422/82.09 , 436/164 , 436/73 , 436/74 , 436/79 , 436/84 , 600/369 , 73/64.41 , 73/64.43

ABSTRACT:

A method which may be used to determine haemostatic

dysfunction in a patient
is carried out by (a) adding a reagent to a test sample, wherein the test
sample includes at least a component of a blood sample from a patient; and then
(b) measuring the formation of a precipitate due to the reaction of the test
sample and the reagent, over time so as to derive a time-dependent measurement
profile, the reagent forming a precipitate in the test sample without causing
substantial fibrin polymerization.

35 Claims, 41 Drawing figures

Exemplary Claim Number: 9

Number of Drawing Sheets: 28

---------- KWIC ---------

Detailed Description Text - DETX (7):
To ensure that no cases of DIC were overlooked, the following criteria was
followed. If (a) an abnormal bi-phasic TW was encountered, or (b) a specific
DIC screen was requested, or (c) if there was a prolongation in either the PT
or APTT in the absence of obvious anticoagulant therapy, a full DIC screen was
performed. This would further include the thrombin time (TT) (normal 10.5-15.5
seconds), fibrinogen (Fgn)(normal 1.5-3.8 g/l) and estimation of D-dimer levels
(normal <0.5 mg/l) on the Nyocard D-Dimer (Nycomed Pharma AS, Oslo, Norway).
Platelet counts (Plt) (normal 150-400 10.sup.9 /l) performed on an EDTA sample
at the same time were recorded. In addition, clinical details were fully
elucidated on any patient with a bi-phasic TW or coagulation abnormalities
consistent with DIC.

US-PAT-NO: 5525477

DOCUMENT-IDENTIFIER: US 5525477 A

TITLE: Method for diagnosing blood clotting disorders

DATE-ISSUED: June 11, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hassouna; Houria I.	Grosse Pointe	MI	N/A	N/A

APPL-NO: 08/ 308948

DATE FILED: September 20, 1994

PARENT-CASE:

This is a continuation of application Ser. No. 08/124,835 filed on Sep. 21, 1993, now abandoned, which is a continuation of Ser. No. 07/700,935, filed May 13, 1991, now abandoned, which is a continuation of Ser. No. 07/379,988, filed Jul. 14, 1989, abandoned.

US-CL-CURRENT: 435/13, 436/69 , 530/381 , 530/382 , 530/383 , 530/384 , 702/108 , 702/19

ABSTRACT:

Assay methods for diagnosing blood clotting disorders are described. The assays use data bases for pooled normal plasma (PNP) and plasma from healthy volunteers, males and females ages 18 to 64 years. Charting on a comparative basis of patient plasma and PNP allows the results to be interpreted by reference to the data base. Simple, rapid, inexpensive and

highly sensitive
and specific assays devised for diagnosing blood clotting disorders are
described.

15 Claims, 31 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 25

---------- KWIC ---------

Detailed Description Text - DETX (21):
(6) Thrombin Clotting Time/Thrombin Time Assay (TCT/TT). TCT or TT is the
same assay given two slightly different names. TCT/TT measures the time taken
by exogenously added thrombin to proteolyze plasma fibrinogen and to form a
clot. TCT/TT assays are not standardized by the prior art. Each laboratory
determines the activity (strength) of thrombin to be used in the assay. It is
customary to adjust the thrombin activity to give a clotting time of 8 to 9
seconds with 0.2 ml citrated pooled normal plasma (PNP). This is equivalent to
1.2 NIH units of thrombin activity.

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=> file medline caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 17:55:42 ON 05 JUN 2003

FILE 'CAPLUS' ENTERED AT 17:55:42 ON 05 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> s thrombin time
L1         2656 THROMBIN TIME

=> s fast closting
L2            0 FAST CLOSTING

=> s fast clotting
L3            4 FAST CLOTTING

=> s l1 (p) (5 seconds)
L4            2 L1 (P) (5 SECONDS)

=> duplicate remove l4
PROCESSING COMPLETED FOR L4
L5             2 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)

=> d l5 1-2 ibib abs

L5   ANSWER 1 OF 2     MEDLINE
ACCESSION NUMBER:    89243862     MEDLINE
DOCUMENT NUMBER:     89243862   PubMed ID: 2497603
TITLE:               Physiological coagulation profile of dairy cattle.
AUTHOR:              Heuwieser W; Biesel M; Grunert E
SOURCE:              ZENTRALBLATT FUR VETERINARMEDIZIN. REIHE A, (1989 Jan) 36
                     (1) 24-31.
                     Journal code: 0331323. ISSN: 0514-7158.
PUB. COUNTRY:        GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         198906
ENTRY DATE:          Entered STN: 19900306
                     Last Updated on STN: 20000303
                     Entered Medline: 19890612
AB   90 clinically healthy cattle with a normal estrus cycle (German Black
     Pied) were investigated.  Normal values for the physiological coagulation
     profile including prothrombin time, partial thromboplastin time,
       ***thrombin***     ***time***  , and fibrinogen concentration were
     determined.  The following ranges of normal values (means +/- 2SD) were
     calculated: prothrombin time (PT) 20.1-30.1 seconds; partial
     thromboplastin time (PTT) 25.3-44.  ***5***     ***seconds***  ;
       ***thrombin***     ***time***   (TT) 12.4-17.2 seconds, and fibrinogen
     concentration 125-697 mg/dl.  During the day and day to day variations in
     the individual parameters of the coagulation profile were not observed.

L5   ANSWER 2 OF 2     MEDLINE
ACCESSION NUMBER:    77151425     MEDLINE
DOCUMENT NUMBER:     77151425   PubMed ID: 850868
TITLE:               The relationship of coagulation factors to clinical
                     complications of acute pancreatitis.
AUTHOR:              Ranson J H; Lackner H; Berman I R; Schinella R
SOURCE:              SURGERY, (1977 May) 81 (5) 502-11.
                     Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         197705
ENTRY DATE:          Entered STN: 19900313
                     Last Updated on STN: 19980206
                     Entered Medline: 19770527
AB   Alterations in coagulation factors have been reported during acute
     pancreatitis.  Therefore the relationship of coagulation measurements to
     complications of pancreatitis was evaluated prospectively in 35 patients
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in whom 130 serial coagulation profiles were performed, consisting of fibrinogen, platelet count (PC), fibrinogen-fibrin-related-antigen (FR-antigen), prothrombin time (PT), partial thromboplastin time, ***thrombin*** ***time*** , euglobulin clot lysis, and Factors II, V and VII-X levels. During attacks of acute pancreatitis, over-all mean initial fibrinogen and PC of 268 mg. per 100 ml. and 214,000 per cubic millimiter rose significantly (p less than 0.005) to peaks of 362 mg. per 100 ml. and 477,800 per cubic millimeter by day 6 to 10. Mean initial FR-antigen of 4.8 microgram per milliliter rose to peak 7.4 microgram per milliliter on day 5. In 21 patients with mild pancreatitis, mean highest fibrinogen, PC, FR-antigen, and PT were 329 mg. per 100 ml., 361,500 per cubic millimeter, 5.3 microng per milliliter and 14.1 seconds. These values were significantly higher (p less than 0.05 to 0.01) in patients with severe pancreatitis, being 422 mg. per 100 ml. 528,000 per cubic millimeter, 13.7 microng per milliliter, and 15. ***5*** ***seconds*** , respectively. Evaluation of the relationship of coagulation measurements to early clinical features showd that mean initial fibrinogen levels were significantly higher (p less than 0.05 to 0.01) in patients with initial amylase greater than 1,000 Somogyi units percent, serum glutamic oxaloacetic transaminase (SGOT) greater than 250 S.F.U. percent, and initial 72 hour PAO2 less than 75 mm. Hg. Early hypoxemia also correlated (p less than 0.05) with elevated initial FR-antigen levels. Impaired early renal function correlated (p less than 0.01) with elevated initial PC only. Early hypocalcemia did not correlate with coagulation measurements. These findings demonstrate that marked changes in coagulation parameters occur during acute pancreatitis and are related to over-all morbidity. Correlation of early coagulation measurements with amylase levels and with respiratory, renal, and hepatic dysfunction suggests that enzyme-related intravascular coagulation may be implicated in the pathogenesis of these complications of pancreatitis.

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=> d his

     (FILE 'HOME' ENTERED AT 17:55:03 ON 05 JUN 2003)

     FILE 'MEDLINE, CAPLUS' ENTERED AT 17:55:42 ON 05 JUN 2003
L1          2656 S THROMBIN TIME
L2             0 S FAST CLOSTING
L3             4 S FAST CLOTTING
L4             2 S L1 (P) (5 SECONDS)
L5             2 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)

=> s l1 (p) (4 seconds)
L6             6 L1 (P) (4 SECONDS)

=> duplicate remove l6
PROCESSING COMPLETED FOR L6
L7             6 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

=> d l7 1-6 ibib abs

L7   ANSWER 1 OF 6     MEDLINE
ACCESSION NUMBER:    2000435070     MEDLINE
DOCUMENT NUMBER:     20433406   PubMed ID: 10977780
TITLE:               Local anticoagulation of the extracorporeal circuit with
                     heparin and subsequent neutralization with protamine during
                     immunoadsorption.
AUTHOR:              Schmaldienst S; Goldammer A; Spitzauer S; Derfler K; Horl W
                     H; Knobl P
CORPORATE SOURCE:    Department of Medicine III, Division of Nephrology and
                     Dialysis, University of Vienna, Austria..
                     sabine@nephro.imed3.akh-wien.ac.at
SOURCE:              AMERICAN JOURNAL OF KIDNEY DISEASES, (2000 Sep) 36 (3)
                     490-7.
                     Journal code: 8110075. ISSN: 1523-6838.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200009
ENTRY DATE:          Entered STN: 20000928
                     Last Updated on STN: 20010521
                     Entered Medline: 20000921
AB   A regimen of local anticoagulation of an immunoadsorption device was
     studied. The extracorporeal circuit was anticoagulated with citrate
     (5.5%) and a continuous infusion of heparin (2,000 U/h or 1,500 U/h),
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which was neutralized by a continuous infusion of protamine chloride (75% of the heparin dose) before reinfusion in 23 patients treated with low-density lipoprotein or immunoglobulin apheresis. Sufficient anticoagulation of the extracorporeal circuit was obtained (activated partial thromboplastin time [APTT] > 180 seconds; ***thrombin*** ***time*** [TT] > 120 seconds; anti-Xa activity, 1.05 +/- 0.21 U/mL) during the entire treatment of 190 minutes, whereas coagulation parameters in the patients' blood stayed within the normal range. In a control group without heparin neutralization, full systemic anticoagulation of the patients occurred (APTT, 157.8 +/- 30.6 seconds; TT, 119.8 +/- 0. ***4*** ***seconds*** ; anti-Xa activity, 0.88 +/- 0.21 U/mL). No side effects or clotting of the system were observed. Our data show that this regimen of local anticoagulation is a safe protocol for extracorporeal circulation without exposing the patients to anticoagulants.

L7 ANSWER 2 OF 6 MEDLINE
ACCESSION NUMBER: 2001202006 MEDLINE
DOCUMENT NUMBER: 20574141 PubMed ID: 11124095
TITLE: The correlation between plasma anti-factor Xa activity and haemostatic tests in healthy dogs, following the administration of a low molecular weight heparin.
AUTHOR: Mischke R; Grebe S
CORPORATE SOURCE: Clinic for Small Animals, School of Veterinary Medicine, Bischofsholer Damm 15, D-30173 Hannover, Germany.
SOURCE: RESEARCH IN VETERINARY SCIENCE, (2000 Dec) 69 (3) 241-7. Journal code: 0401300. ISSN: 0034-5288.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010417 Last Updated on STN: 20010417 Entered Medline: 20010412

AB The aim of the study was to examine how activated partial thromboplastin time (APTT, two different reagents), ***thrombin*** ***time*** (TT, thrombin activity in the reagent: 3 or 6 IU ml(-1)) and reaction time of the resonance thrombogram (RTG-r) in healthy dogs are influenced by low molecular weight heparin (LMWH). Three different LMWH doses were given subcutaneously or intravenously to groups, each of five healthy dogs. Mean plasma anti-FXa activities of 0.43, 0.88 and 1.86 anti-FXa IU ml(-1)were measured 2 min after intravenous injection of 25, 50 or 100 anti-FXa IU kg(-1). At this time, a dose-dependent increase of the coagulation times, above the baseline values ($P < 0.05$), was observed for all haemostatic tests. The significant prolongation of coagulation time lasted 10 minutes to 3 hours, and it was dependent on the test employed and LMWH dose. After subcutaneous LMWH injection of 50, 100 and 200 anti-FXa IU kg(-1), significant changes of the coagulation time above initial values were limited to the period around the time when maximum anti-FXa activities (0.23, 0.43 or 0.90 anti-FXa IU ml(-1)) were observed. For the tests which were less affected by the LMWH (APTT, TT([6 IU ml)(-1)(])), only small increases (< ***4*** ***seconds***) were observed even after the highest subcutaneous LMWH dose. The correlation between plasma heparin activity and the relative alteration compared to the initial value (ratio), of the different coagulation tests was only moderate and considerably lower for RTG-r (r(s)= 0.526) than for the TT (r(s)= 0.711([6 IU ml(-1)]), r(s)= 0.780([3 IU ml(-1)])) and APTT (r(s)= 0.667([reagent 1]), r(s)= 0.727([reagent 2])). The low degree of prolongation, which was found particularly for the group tests APTT and TT([6 IU ml)(-1)]), reflects the low anti-thrombin activity of LMWH. The results indicate that measurement of anti-FXa activity with chromogenic substrates is the method of choice to control LMWH therapy in dogs, as is the case in humans.

L7 ANSWER 3 OF 6 MEDLINE
ACCESSION NUMBER: 95315635 MEDLINE
DOCUMENT NUMBER: 95315635 PubMed ID: 7795307
TITLE: Factor XII deficiency and cardiopulmonary bypass.
AUTHOR: Wallock M; Arentzen C; Perkins J
CORPORATE SOURCE: Department of Cardiovascular Surgery, Evanston Hospital, IL 60201, USA.
SOURCE: PERFUSION, (1995) 10 (1) 13-6. Journal code: 8700166. ISSN: 0267-6591.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950817
Last Updated on STN: 19950817
Entered Medline: 19950803

AB Factor XII initiates the intrinsic coagulation cascade and may affect the fibrinolytic system. Routine coagulation tests used during cardiopulmonary bypass (CPB) are abnormal in factor-XII-deficient patients and are useless for monitoring anticoagulation in these patients. A factor-XII-deficient patient requiring CPB is described. The baseline celite activated clotting time (ACT) was greater than 1400 seconds and the ***thrombin*** ***time*** was 12. ***4*** ***seconds*** (control, 11.9 seconds). Two units of plasma were given resulting in an ACT of 173 seconds. Following 300 units/kg of heparin and during CPB, the ACT ranged from 670-596 seconds with the ***thrombin*** ***time*** greater than 200 seconds. Plasma provides exogenous factor XII allowing an endpoint on the ACT test and may protect against possible postoperative hypofibrinolytic complications. A commercially available modified ***thrombin*** ***time*** may also be useful and provide an endpoint during high-dose heparinization.

L7 ANSWER 4 OF 6 MEDLINE
ACCESSION NUMBER: 90342490 MEDLINE
DOCUMENT NUMBER: 90342490 PubMed ID: 2116709
TITLE: Coagulation profile in different stages of pregnancy and under consideration of placental expulsion in dairy cattle.
AUTHOR: Heuwieser W; Kautni J; Grunert E
CORPORATE SOURCE: Clinic of Obstetrics and Gynecology of Cattle, School of Veterinary Medicine, Hannover, FRG.
SOURCE: ZENTRALBLATT FUR VETERINARMEDIZIN. REIHE A, (1990 May) 37 (4) 310-5.
Journal code: 0331323. ISSN: 0514-7158.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901012
Last Updated on STN: 20000303
Entered Medline: 19900911

AB It was the aim of the present study to determine different parameters of blood coagulation in dairy cattle in the course of gestation (n = 19) and during 9 days post partum (n = 40). The coagulation profile comprised prothrombin time, partial thromboplastin time, ***thrombin*** ***time*** , fibrinogen concentration, and platelet count. Prothrombin time was shorter in the 2nd month of gestation (13.9 s) than in the 7th (15.2 s) month. A reduction of partial thromboplastin time towards the end of gestation by approximately ***4*** ***seconds*** was statistically insignificant (p greater than 0.05). A significant change of fibrinogen concentration was established over a period of 10 days ante partum. Immediately before parturition, fibrinogen level (484 mg/dl) increased compared to one (325 mg/dl) and two (343 mg/dl) days before calving. Cows whose calves were developed per vias naturales displayed pronounced differences of fibrinogen concentration. Animals with retained placenta showed significantly higher fibrinogen concentrations than cows with normal expulsion of the placenta on all days.

L7 ANSWER 5 OF 6 MEDLINE
ACCESSION NUMBER: 84125317 MEDLINE
DOCUMENT NUMBER: 84125317 PubMed ID: 6582779
TITLE: A heparin-like anticoagulant in an 8-month-old boy with acute monoblastic leukemia.
AUTHOR: Bussel J B; Steinherz P G; Miller D R; Hilgartner M W
CONTRACT NUMBER: CA23472 (NCI)
SOURCE: AMERICAN JOURNAL OF HEMATOLOGY, (1984 Jan) 16 (1) 83-90.
Journal code: 7610369. ISSN: 0361-8609.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198403
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840301

AB An 8-month-old male with acute monoblastic leukemia died during induction chemotherapy of severe bleeding refractory to repeated infusions of

platelets and clotting factors. A heparin effect was suggested by prothrombin time (PT) of 26 seconds, partial thromboplastin time (PTT) of 94 seconds, ***thrombin*** ***time*** 240 seconds, and reptilase time 18. ***4*** ***seconds*** , with a fibrinogen of 88 mg/dl. Both plasma mixed with the patient's urine and the patient's plasma had their ***thrombin*** ***times*** corrected toward normal by both PF4 and protamine. Synergism of the anticoagulant with antithrombin III was demonstrated not only by enhanced inhibition of thrombin but also by an increased rate of formation of thrombin--antithrombin III complexes in the presence of the anticoagulant, which was eliminated by preincubation with heparinase. Since the anticoagulant activity was not found in the blasts themselves, it is presumed that the anticoagulant is heparin/heparan liberated from the endothelial lining by products of the cell destruction secondary to chemotherapy.

L7 ANSWER 6 OF 6 MEDLINE
ACCESSION NUMBER: 76271538 MEDLINE
DOCUMENT NUMBER: 76271538 PubMed ID: 822526
TITLE: Exchange transfusion and major surgery in acute hepatic failure.
AUTHOR: Silva Y J; Parameswaran P G; James P
SOURCE: SURGERY, (1976 Sep) 80 (3) 343-9.
Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197610
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19970203
Entered Medline: 19761020

AB Of the many techniques available for short-term support of the failing liver, a closed "isovolemic" method of exchange transfusions remains simple and safe. We used this method to exchange 143 U. of blood in eight patients in Stage III/IV hepatic failure; four patients had no previous underlying liver disease. Significant improvements of biochemical and coagulation parameters resulted. Serum bilirubin, glutamic oxaloacetic transaminase and, lactic dehydrogenase levels fell from a mean, 24.7 mg. per 100 ml., 3,100 mU. per milliliter, 2,796 mU. per millilter, respectively, to 10.9 mg. per 100 ml., 122.9 mU. per milliliter, and 558.5 mU. per milliliter, respectively, 6 to 12 hours following transfusion. Prolongation of serum prothrombin and ***thrombin*** ***times*** (over controls) of 31.1 and 30.1 seconds (mean) were markedly decreased to 3.2 and 6.1 seconds 6 to 12 hours following transfusion; partial thromboplastin times were decreased from a mean 196. ***4*** ***seconds*** to 87.8 seconds after the same period. Levels of Factors VII, IX, and X were increased transiently. Correlations of exchange transfusion to reversal of coma and improvements in electroencephalograms were poor. Two patients in coma were subjected to major surgery following exchange transfusion; one patient survived vagotomy and hemigastrectomy for stress bleeding and one withstood a temporary baboon liver heterotopic transplant which aided in recovery from coma. We recommend isovolemic exchange transfusion as specific treatment for coagulation abnormalities and as an over-all aid in lowering the mortality rate of patients in hepatic coma. Marked improvements in homeostasis make major surgery feasible.

=> d his

(FILE 'HOME' ENTERED AT 17:55:03 ON 05 JUN 2003)

FILE 'MEDLINE, CAPLUS' ENTERED AT 17:55:42 ON 05 JUN 2003
L1 2656 S THROMBIN TIME
L2 0 S FAST CLOSTING
L3 4 S FAST CLOTTING
L4 2 S L1 (P) (5 SECONDS)
L5 2 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)
L6 6 S L1 (P) (4 SECONDS)
L7 6 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

=> s l1 (p) l3
L8 0 L1 (P) L3

=> s l1 (p) short
L9 43 L1 (P) SHORT

```
=> s l9 (p) seconds
L10             1 L9 (P) SECONDS

=> d l10 1 ibib abs

L10  ANSWER 1 OF 1     MEDLINE
ACCESSION NUMBER:    76271538     MEDLINE
DOCUMENT NUMBER:     76271538   PubMed ID: 822526
TITLE:               Exchange transfusion and major surgery in acute hepatic
                     failure.
AUTHOR:              Silva Y J; Parameswaran P G; James P
SOURCE:              SURGERY, (1976 Sep) 80 (3) 343-9.
                     Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         197610
ENTRY DATE:          Entered STN: 19900313
                     Last Updated on STN: 19970203
                     Entered Medline: 19761020
AB   Of the many techniques available for   ***short***  -term support of the
     failing liver, a closed "isovolemic" method of exchange transfusions
     remains simple and safe.  We used this method to exchange 143 U. of blood
     in eight patients in Stage III/IV hepatic failure; four patients had no
     previous underlying liver disease.  Significant improvements of
     biochemical and coagulation parameters resulted.  Serum bilirubin,
     glutamic oxaloacetic transaminase and, lactic dehydrogenase levels fell
     from a mean, 24.7 mg. per 100 ml., 3,100 mU. per milliliter, 2,796 mU. per
     millilter, respectively, to 10.9 mg. per 100 ml., 122.9 mU. per
     milliliter, and 558.5 mU. per milliliter, respectively, 6 to 12 hours
     following transfusion.  Prolongation of serum prothrombin and
       ***thrombin***     ***times***   (over controls) of 31.1 and 30.1
       ***seconds***   (mean) were markedly decreased to 3.2 and 6.1
       ***seconds***   6 to 12 hours following transfusion; partial
     thromboplastin times were decreased from a mean 196.4   ***seconds***   to
     87.8   ***seconds***   after the same period.  Levels of Factors VII, IX,
     and X were increased transiently.  Correlations of exchange transfusion to
     reversal of coma and improvements in electroencephalograms were poor.  Two
     patients in coma were subjected to major surgery following exchange
     transfusion; one patient survived vagotomy and hemigastrectomy for stress
     bleeding and one withstood a temporary baboon liver heterotopic transplant
     which aided in recovery from coma.  We recommend isovolemic exchange
     transfusion as specific treatment for coagulation abnormalities and as an
     over-all aid in lowering the mortality rate of patients in hepatic coma.
     Marked improvements in homeostasis make major surgery feasible.


=> d his

     (FILE 'HOME' ENTERED AT 17:55:03 ON 05 JUN 2003)

     FILE 'MEDLINE, CAPLUS' ENTERED AT 17:55:42 ON 05 JUN 2003
L1          2656 S THROMBIN TIME
L2             0 S FAST CLOSTING
L3             4 S FAST CLOTTING
L4             2 S L1 (P) (5 SECONDS)
L5             2 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)
L6             6 S L1 (P) (4 SECONDS)
L7             6 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
L8             0 S L1 (P) L3
L9            43 S L1 (P) SHORT
L10            1 S L9 (P) SECONDS

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    26.09      26.30

STN INTERNATIONAL LOGOFF AT 18:00:49 ON 05 JUN 2003
```

PRODUCT NUMBER			US $
	THR-GLN	25 mg	25.85
T3275	*[96337-79-0]* $C_9H_{17}N_3O_5$		
-0°C	FW 247.3		
	THR-LEU	100 mg	10.90
T 8400	*[50299-12-2]* $C_{10}H_{20}N_2O_4$	250 mg	21.60
-0°C	FW 232.3	1 g	64.50

THR-LYS-PRO
See: Tuftsin Fragment 1-3 under Bioactive Peptides
Page 1165

THROMBIN
(EC 3.4.21.5)
Serine protease which selectively cleaves Arg-Gly bonds in fibrinogen to form fibrin and fibrinopeptides A and B.
Unit Definition: Activity is expressed in NIH units obtained by direct comparison to a NIH Thrombin Reference Standard, Lot J. The NIH assay procedure uses 0.2 ml diluted plasma (1:1 with saline) as a substrate and 0.1 ml of thrombin sample (stabilized in a 1% buffered albumin solution) based on a modification of the method of Biggs. Only clotting times in the range of 15-25 seconds are used for determining thrombin concentrations
Human source material has tested negative for HIV and HBsAg
Ref.: Human Blood Coagulation, Haemostasis and Thrombosis, 2nd ed., R. Biggs, Editor, Blackwell Scientific Publications, Philadelphia, 1976, p 722.
[9002-04-4]

T 3399	**From Bovine Plasma**	1,000 units	17.85
-0°C	**Lyophilized powder**	10,000 units	125.75
	containing approx. 50% protein (Biuret); balance primarily sodium chloride and Tris-HCl.		
	Activated with rabbit brain thromboplastin.		
	Activity: 50-150 NIH units per mg protein.		
4648	**From Bovine Plasma**	1,000 units	16.30
0°C	**Lyophilized powder**	10,000 units	114.45
	containing approx. 50% protein; balance primarily sodium chloride and Tris-HCl, pH 7.0	100,000 units	718.20
	Activated with bovine brain thromboplastin		
	Activity: 50-175 NIH units per mg protein (Biuret).		
9000	**From Bovine Plasma**	500 units	63.10
°C	Frozen solution of a crude preparation containing approximately 1,000 NIH units per ml in 0.05 M phosphate buffer, pH 7.0.	2,500 units	187.90
		Shipped in dry ice	
	Activity: Minimum 125 NIH units per mg protein (Biuret).		
1265	**From Bovine Plasma**	500 units	30.00
C	**Lyophilized powder**	2,500 units	103.65
	containing approx. 25% protein and 75% sodium citrate, pH 5.8.	10,000 units	297.45
		25,000 units	501.20
	Activity: 175-350 NIH units per mg protein (Biuret).		
681	**From Bovine Plasma**	5,000 units	163.05
C	**Lyophilized from Tris buffer and sodium chloride.**		
	Activity: Minimum 700 NIH units per mg protein (Bradford).		
634	**From Bovine Plasma**	100 units	27.40
C	Lyophilized from saline sodium citrate buffer, pH 6.5	250 units	53.65
		500 units	79.65
	Activity: 600-1,500 NIH units per mg protein (Biuret).	1,000 units	148.25
	Essentially free of other known clotting factors (non-activated and activated) as well as plasminogen and plasmin.		

(Continued)

PRODUCT NUMBER			US $
	(Continuation of) **THROMBIN**		
T 7513	**From Bovine Plasma**	50 units	33.80
-0°C	Lyophilized from saline sodium citrate buffer, pH 6.5	100 units	55.35
		250 units	104.10
	Activity: 1,500-2,500 NIH units per mg protein ($E^{1\%}_{280}$ = 19.5).	500 units	193.95
	Essentially free of other known clotting factors (non-activated and activated) as well as plasminogen and plasmin.		
	See also: Tissue Culture Media and Reagents		
	Page 1794		
T 7009	**From Human Plasma**	100 units	36.15
-0°C	Lyophilized from saline sodium citrate buffer, pH 6.5	250 units	71.05
		1,000 units	186.20
	Activity: Approx. 1,000 NIH units per mg protein ($E^{1\%}_{280}$ = 18.3).	5,000 units	703.50
	Essentially free of other known clotting factors (non-activated and activated) as well as plasminogen and plasmin.		
	See also: Tissue Culture Media and Reagents		
	Page 1794		
T 9135	**From Human Plasma**	10 vials	48.60
-0°C	**Lyophilized powder**		
	Prepared from Product No. T 7009		
	Minimum 10 NIH units per vial, for routine use in the thrombin time test.		
	Bovine albumin added as stabilizer.		
T 6884	**From Human Plasma**	100 units	39.60
-0°C	Lyophilized from saline sodium citrate buffer, pH 6.5	250 units	87.00
		1,000 units	179.90
	Activity: Approx. 2,000 NIH units per mg protein ($E^{1\%}_{280}$ = 18.3).	5,000 units	733.00
	Essentially free of other known clotting factors (non-activated and activated) as well as plasminogen and plasmin.		
T 9010	**From Human Plasma**	10 vials	52.95
-0°C	**Lyophilized powder**		
	Prepared from Product No. T 6884		
	Minimum 10 NIH units per vial, for routine use in the thrombin time test.		
	Bovine albumin added as stabilizer.		
T 1063	**From Human Plasma**	250 units	87.80
-0°C	Lyophilized from 0.02 M Bis/Tris buffer, pH 6.5, 0.15 M NaCl and 0.1% PEG-8000.	1,000 units	180.60
	Activity: >2800 units per mg protein ($E^{1\%}_{280}$ = 18.3).		
T 8885	**From Human Plasma**	10 vials	57.90
-0°C	**Lyophilized powder**	25 vials	122.90
	Minimum 10 NIH units per vial, for routine use in the thrombin time test.		
	Bovine albumin added as stabilizer.		
T 0553	**From Human Plasma**	250 units	43.10
-0°C	**Lyophilized powder**	1,000 units	119.55
	containing approx. 35% protein (Biuret); balance primarily sodium chloride and Tris-HCl.		
	Activity: 50-300 NIH units per mg protein.		
T 9677	**From Human Plasma**	250 units	57.60
-0°C	**Lyophilized powder**	1,000 units	159.75
	Technical Grade		
	Activity: 50-300 NIH units per mg protein		

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